STOHASTIČKI MODEL STANIČNIH REAKCIJSKIH SUSTAVA

STOHASTIC MODEL OF CELL REACTION SYSTEMS

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Mathematical modelling of microbial cells can be developed by application of chemical engineering principles of mass and energy balances for chemical reactors. Cell as a reactor is a viewed as a multiphase catalytic reactor with an expanding volume due to growth, with about $50 \cdot 10^6$ molecules, 10^5 reactions, and with hierarchical organised and spatially distributed internal control systems. The robust approach to modelling is based on standard chemical engineering picture of a well mixed cup with deterministic kinetics. However, due to small number of individual molecules present in a cell, stochastic effects in molecular interactions become important. Application of Gillespie [1] algorithm for exact simulation of stochastic chemical reaction systems can be applied for computer cell simulation. Stochastic models are formulated by translation of deterministic mechanisms and kinetic parameters into evaluation of probabilities of individual molecular interactions. It is, like in chemical engineering, a "scale down procedure", where kinetic parameters are experimentally determined in large systems (deterministic, "in vitro" enzyme reactors), and than are extrapolated down to the molecular level (cells). Such stochastic modelling provides deterministic solutions as an asymptotic case of a stochastic model. However, this is an "ad hoc" procedure which may be hopefully resolved by computer simulation and experimental molecular biology. In this work are by computer simulation analysed stochastic interactions on Michaelis-Menten mechanism, oscillatory Lotka-Volterra reactions, and cell infection by hepatitis-C virus [2-3]. W.R. *Mathematica* software language and numerical procedure are applied. The analysis is focused on determination of bifurcation conditions between stochastic and deterministic behaviour, stochastic effects on critical stability, and development of chaos.

[1] Gillespie, D.T., J. Phys. Chem., **81** (1977) 2340-2361.
[2] Gend van, C,, Kummer, U., Proceedings of the 2-nd International Conference on System Biology (Eds. Yi, Hucka, Morohaski, Kitomo), Omnipress, Madison, USA, 2001, 326-333.
[3] Shimizu, T.S., Bray D., Computational Cell Biology - The Stochastic Approach, MIT Press, Boston, 2002, 22-56.